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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/508,418	06/08/2000	MAMORU HORIKOSHI	Q58140	1158

7590 08/09/2002

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EXAMINER
STEADMAN, DAVID J

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 08/09/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/508,418	HORIKOSHI ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 June 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 7-26* is/are pending in the application.

4a) Of the above claim(s) *9-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,7 and 8* is/are rejected.

7)☒ Claim(s) *2 and 5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

Claims 1-5 and 7-26 are pending.

Applicants' amendment to the title of the specification and claims 1-5, 7, and 8 and cancellation of claim 6 in Paper No. 20, filed 06/05/02 is acknowledged.

Claims 9-26 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim.

Applicants' arguments filed in Paper No. 20 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Drawings

1. Applicants' submission of formal drawings in Paper No. 18 is acknowledged. The corrected drawings have been reviewed and approved by the Draftsperson. Direct any inquiries concerning drawing review to the Drawing Review Branch (703) 305-8404.

Claim Rejections - 35 USC § 112, Second Paragraph

2. Claim 3 and 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. The rejection of claims 3 and 4 as being indefinite in the recitation of the term "a transit peptide is deleted" is maintained. The rejection was fully explained in a previous Office action.

Applicants argue at page 8 of the response filed as Paper No. 20 that the definition of a "transit peptide" has been provided at page 3 of the instant specification. Applicants argue a skilled artisan could determine which amino acids of SEQ ID NO:2 form the "transit peptide" and that the recitation of "transit

peptide" is sufficiently clear such that a skilled artisan would not require the identification of specific amino acids of SEQ ID NO:2 in order to determine which of those amino acids is the "transit peptide". Applicants' argument has been fully considered but is not found persuasive to overcome the instant rejection. The definition of "transit peptide" as provided at page 3 of the instant specification provides no indication as to the scope of amino acids that are encompassed by the term "transit peptide". As such, a skilled artisan would not recognize the amino acids of SEQ ID NO:2 that are considered by applicant to be a "transit peptide". It is suggested that applicants identify the amino acids of SEQ ID NO:2 that are considered to be a "transit peptide".

4. Claim 4 recites the limitation "said purified protoporphyrinogen oxidase" in line 4. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 112, First Paragraph

5. Claims 1-5, 7, and 8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. Claims 1 (claims 2-4, 7, and 8 dependent therefrom) recite the limitation "tolerance to pyrazole compounds". Applicants' response identifies support (page 5) for this limitation at pages 24 and 25 of the specification. However, the examiner can find support only for a mutated peptide having resistance to the pyrazole compounds listed in claim 7. The examiner can find no support in the specification, claims, or drawings as originally filed for a mutated peptide as set forth in claim 1 having tolerance to *all* pyrazole compounds equivalent to that of SEQ ID NO:2. Therefore, this limitation is considered new matter.

6. The written description rejection of claims 1, 3, 7, and 8 under 35 U.S.C. 112, first paragraph, is maintained. The rejection was fully explained in a previous Office action. Applicants argue the claims have been amended to more clearly define the claimed invention. Applicants' argument has been fully considered but is not found persuasive to overcome the instant rejection.

Claim 1 encompasses all protox polypeptides tolerant to photobleaching herbicide and a tolerance to pyrazole compounds equivalent to SEQ ID NO:2. Claim 3 (claims 7 and 8 dependent therefrom) encompasses all protox polypeptides tolerant to photobleaching herbicide with a deleted transit peptide and a tolerance to pyrazole compounds equivalent to SEQ ID NO:2. The specification fails to provide a sufficient description of the claimed genus of protox polypeptides as it merely describes the functional features of the genus without providing any definition of the structural features of the species within the genus. The CAFC in *UC California v. Eli Lilly*, (43 USPQ2d 1398) stated that: "In claims to genetic material, however a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA", without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus". Similarly with the claimed genus of protox polypeptides, the functional definition of the genus does not provide any structural information commonly possessed by members of the genus that distinguish the polypeptide species within the genus from other proteins such that one can visualize or recognize the identity of the members of the genus. Given this lack of description of representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

7. The scope of enablement rejection of claims 1, 3, 7 and 8 under 35 U.S.C. 112, first paragraph, is maintained. The rejection was fully explained in a previous Office action. Applicants argue the claims the claims have been amended to more clearly define the claimed invention. Applicants' argument has been fully considered but is not found persuasive to overcome the instant rejection.

The scope of claimed protox polypeptides is not commensurate with the enablement provided by the instant specification, which provides enablement only for the protox polypeptide of SEQ ID NO:2.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re* Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s). Claims 1 and 3 are so broad as to encompass *any* protox polypeptide tolerant to photobleaching herbicide and having tolerance to *any* pyrazole compounds equivalent to that of SEQ ID NO:2 (claim 1) with a deleted transit peptide (claim 3). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. At the time of the invention, the ability of a skilled artisan to generate mutations in a protein's amino acid sequence with an expectation of obtaining the desired biological activity was highly unpredictable. While the ability to generate mutations in a protein's amino acid sequence is known in the art, the ability to generate a mutation within a protein's amino acid sequence to elicit a desired function, in this case tolerance to photobleaching herbicide and tolerance to all pyrazole compounds equivalent to that of SEQ ID NO:2, requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. The specification provides guidance and working examples only for the polypeptide of SEQ ID NO:2. Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of the protox polypeptide of SEQ ID NO:2 or SEQ ID NO:2 with a deleted transit peptide resulting in tolerance to photobleaching herbicide and tolerance to *any* pyrazole compound equivalent to that of SEQ ID NO:2. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is

unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

8. The rejection of claims 1, 3, 7, and 8 under 35 U.S.C. 102(b) as being anticipated by Ward et al. (WO95/34659; hereafter referred to as "Ward") is maintained. The rejection was fully explained in a previous Office action. Applicants argue the claimed protox polypeptide is distinct from that disclosed by Ward. Applicants argue Ward teaches *A. thaliana* and *Z. mays* protox polypeptides and does not teach an *N. tabacum* protox polypeptide. Applicants' argument is not found persuasive. It is noted that applicants argue limitations that are not present in the rejected claims. Claims 1, 3, 7, and 8 do not limit the source of the protox polypeptide and are therefore not limited to a *N. tabacum* protox polypeptide. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicants further argue the mutant protox polypeptides of Ward achieved only a 10-fold increase in herbicide resistance relative to the wild type polypeptides, while the polypeptides disclosed in the instant specification achieved a significantly greater resistance to photobleaching herbicide as demonstrated by Table 6 at page 25 of the specification. Applicants' argument is not found persuasive. Applicants compare herbicide resistance between the *A. thaliana* protox mutant of Ward having an alanine to valine substitution at position 220 and the protox of SEQ ID NO:2 of the instant application. Applicants' results indicate that SEQ ID NO:2 has a greater herbicide resistance relative to the *A. thaliana* protox Val220Ala mutant of Ward. However, Ward teaches other mutants of *A. thaliana* protox (page 65) as well. Ward teaches these mutants exhibit *at least* 10-fold more herbicide resistance (page 65, bottom). Therefore, it is not clear as to whether the other mutant protox polypeptides of Ward have or do not have an equivalent resistance to all pyrazole compounds as that of SEQ ID NO:2. As such, applicants have not demonstrated a distinguishing characteristic or characteristics between the claimed protox enzymes and the protox enzymes of the prior art. Since the Office does not have the facilities for

examining and comparing applicants' protein with all mutant protox polypeptides as disclosed by Ward, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See *In re* Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re* Fitzgerald et al., 205 USPQ 594.

9. The rejection of claims 1, 3, and 6 under 35 U.S.C. 102(e) as being anticipated by Volrath et al. (US Patent 5,939,602; hereafter referred to as "Volrath") is maintained. The rejection was fully explained in a previous Office action. Applicants argue Volrath fails to disclose all limitations of the rejected claims because Volrath does not disclose a protox having an enzyme activity equivalent to SEQ ID NO:2. Applicants argue the specification provides experimental evidence measuring protox activity and also provides data demonstrating resistance pyrazole compounds A-E. Applicants' argument is not found persuasive. It is noted that the term "a mutated peptide... ...having an enzyme activity... ...equivalent to that of said protophorphyyrinogen oxidase" has been interpreted by the examiner in its broadest interpretation, i.e., a polypeptide having protox activity. The specification provides no indication that the term is meant to be interpreted as a polypeptide having an enzymatic rate or specific activity equivalent to that of SEQ ID NO:2. Furthermore, as stated above, the Office does not have the facilities for examining and comparing applicants' protein with the protein of Volrath. Therefore, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See *In re* Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re* Fitzgerald et al., 205 USPQ 594.

Claim Rejections - 35 USC § 103

10. Upon reconsideration of the rejection of claims 1-8 under 35 U.S.C. 103(a) as being unpatentable over Ward in view of Lermontova et al. (Proc Natl Acad Sci 94:8895-8900; hereafter referred to as "Lermontova") is withdrawn. While there is a clear motivation to generate an herbicide-resistant mutant

of the *N. tabacum* protox isoenzyme I as taught by Lermontova, it is unclear as to whether one of ordinary skill in the art would have a reasonable expectation of success for mutating the amino acid sequence of Lermontova according to the corresponding mutation as taught by Ward to generate an herbicide-resistant protox polypeptide. While the sequence of Lermontova shares 71.2 % sequence homology with *A. thaliana* protox, the expectation that the mutation as taught by Ward, i.e., Ala220Val, when performed at corresponding alanine 231 of *N. tabacum* protox isoenzyme I, would result in an increased herbicide resistance is unpredictable. Therefore, the rejection is withdrawn.

Conclusion

11. No claim is in condition for allowance.

Applicant's amendment to claims 1 and 4 necessitated the new ground(s) of rejection presented in this office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Friday from 7:30 am to 2:00 pm and from 3:30 pm to 5:30 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600